

WHAT IS CLAIMED IS:

1           1.     A vascular prosthesis comprising:  
2                   an expandable structure which is implantable within a body lumen; and  
3                   means on or within the structure for releasing mizoribine into the body lumen  
4                   to inhibit smooth muscle cell proliferation.

1           2.     A prosthesis as in claim 1, wherein mizoribine is released at a rate  
2     between 5 µg/day to 200 µg/day.

1           3.     A prosthesis as in claim 1, wherein mizoribine is released at a rate  
2     between 10 µg/day to 60 µg/day.

1           4.     A prosthesis as in claim 1, wherein mizoribine is released at an initial  
2     phase wherein a rate of mizoribine release is between 0 µg/day to 50 µg/day and a subsequent  
3     phase wherein a rate of mizoribine release is between 5 µg/day to 200 µg/day.

1           5.     A prosthesis as in claim 1, wherein mizoribine is released at an initial  
2     phase wherein a rate of mizoribine release is between 5 µg/day to 30 µg/day and a subsequent  
3     phase wherein a rate of mizoribine release is between 10 µg/day to 100 µg/day.

1           6.     A prosthesis as in claim 1, wherein mizoribine is released at an initial  
2     phase wherein a rate of mizoribine release is between 40 µg/day to 300 µg/day and a  
3     subsequent phase wherein a rate of mizoribine release is between 1 µg/day to 100 µg/day.

1           7.     A prosthesis as in claim 1, wherein mizoribine is released at an initial  
2     phase wherein a rate of mizoribine release is between 40 µg/day to 200 µg/day and a  
3     subsequent phase wherein a rate of mizoribine release is between 10 µg/day to 40 µg/day.

1           8.     A prosthesis as in claim 1, wherein mizoribine is released at a constant  
2     rate between 5 µg/day to 200 µg/day.

1           9.     A prosthesis as in claim 1, wherein a total amount of mizoribine  
2     release is in a range from 100 µg to 10 mg.

1           10.    A prosthesis as in claim 1, wherein a total amount of mizoribine  
2     release is in a range from 300 µg to 2 mg.

1                   11.    A prosthesis as in claim 1, wherein a total amount of mizoribine  
2 release is in a range from 500 µg to 1.5 mg.

1                   12.    A prosthesis as in claim 1, wherein a mammalian tissue concentration  
2 of mizoribine at an initial phase is within a range from 0 µg/mg of tissue to 100 µg/mg of  
3 tissue.

1                   13.    A prosthesis as in claim 1, wherein a mammalian tissue concentration  
2 of mizoribine at an initial phase is within a range from 0 µg/mg of tissue to 10 µg/mg of  
3 tissue.

1                   14.    A prosthesis as in claim 1, wherein a mammalian tissue concentration  
2 of mizoribine at a subsequent phase is within a range from 1 picogram/mg of tissue to 100  
3 µg/mg of tissue.

1                   15.    A prosthesis as in claim 1, wherein a mammalian tissue concentration  
2 of mizoribine at a subsequent phase is within a range from 1 nanogram/mg of tissue to 10  
3 µg/mg of tissue.

1                   16.    A prosthesis as in claim 1, wherein the expandible structure is a stent or  
2 graft.

1                   17.    A prosthesis as in claim 1, wherein the means for releasing mizoribine  
2 comprises a matrix formed over at least a portion of the structure.

1                   18.    A prosthesis as in claim 17, wherein the matrix is composed of a  
2 material which undergoes degradation.

1                   19.    A prosthesis as in claim 17, wherein the matrix is composed of a  
2 nondegradable material.

1                   20.    A prosthesis as in claim 19, wherein mizoribine is released by  
2 diffusion through the nondegradable matrix.

1                   21.    A prosthesis as in claim 17, wherein the matrix comprises multiple  
2 layers, wherein at least one layer contains mizoribine and another layer contains mizoribine,  
3 at least one substance other than mizoribine, or no substance.

1                   22. A prosthesis as in claim 21, wherein the at least one substance other  
2 than mizoribine is an immunosuppressive substance selected from the group consisting of  
3 rapamycin, mycophenolic acid, riboflavin, tiazofurin, methylprednisolone, FK 506, zafurin,  
4 and methotrexate.

1                   23. A prosthesis as in claim 21, wherein the at least one substance other  
2 than mizoribine is an agent selected from the group consisting of anti-platelet agent, anti-  
3 thrombotic agent, and IIb/IIIa agent.

1                   24. A prosthesis as in claim 1, wherein the means for releasing mizoribine  
2 comprises a rate limiting barrier formed over at least a portion of the structure.

1                   25. A prosthesis as in claim 24, wherein mizoribine is released by  
2 diffusion through the rate limiting barrier.

1                   26. A prosthesis as in claim 1, wherein the means for releasing mizoribine  
2 comprises a reservoir on or within the structure containing mizoribine and a cover over the  
3 reservoir.

1                   27. A prosthesis as in claim 1, wherein mizoribine is on or within the  
2 expandible structure.

1                   28. A prosthesis as in claim 1, wherein mizoribine is disposed within a  
2 matrix or rate limiting membrane.

1                   29. A vascular prosthesis comprising:  
2                   an expandible structure which is implantable within a body lumen; and  
3                   a rate limiting barrier on the structure for releasing mizoribine into the body  
4 lumen to inhibit smooth muscle cell proliferation;  
5                   wherein the barrier comprises multiple layers, each layer comprising parylast  
6 or paralene and having a thickness in a range from 50 nm to 10 microns.

1                   30. A prosthesis as in claim 29, wherein mizoribine is released at a rate  
2 between 5 µg/day to 200 µg/day.

1                   31. A prosthesis as in claim 29, wherein mizoribine is released at a rate  
2 between 10 µg/day to 60 µg/day.

1                   32.     A prosthesis as in claim 29, wherein at least one layer contains  
2     mizoribine and another layer contains mizoribine, at least one substance other than  
3     mizoribine, or no substance.

1                   33.     A vascular prosthesis comprising:  
2                   an expansible structure;  
3                   a source of mizoribine on or within the structure, wherein the mizoribine is  
4     released from the source when the expansible structure is implanted in a blood vessel; and  
5                   a source of at least one other substance in addition to mizoribine on or within  
6     the structure, wherein the at least one additional substance is released from the source when  
7     the expansible structure is implanted in a blood vessel.

1                   34.     A prosthesis as in claim 33, wherein the at least one additional  
2     substance is an immunosuppressive substance selected from the group consisting of  
3     rapamycin, mycophenolic acid, riboflavin, tiazofurin, methylprednisolone, FK 506, zafurin,  
4     and methotrexate.

1                   35.     A prosthesis as in claim 33, wherein the at least one additional  
2     substance comprises at least one agent selected from the group consisting of anti-platelet  
3     agent, anti-thrombotic agent, and IIb/IIIa agent.

1                   36.     A prosthesis as in claim 33, wherein each source comprises a matrix,  
2     rate limiting membrane, or reservoir.

1                   37.     A method for inhibiting restenosis in a blood vessel following  
2     recanalization of the blood vessel, said method comprising:  
3                   implanting a vascular prosthesis in the blood vessel; and  
4                   releasing mizoribine into the blood vessel so as to inhibit smooth muscle cell  
5     proliferation.

1                   38.     A method as in claim 37, wherein mizoribine is released at a rate  
2     between 5  $\mu$ g/day to 200  $\mu$ g/day.

1                   39.     A method as in claim 37, wherein mizoribine is released at a rate  
2     between 10  $\mu$ g/day to 60  $\mu$ g/day.

1                   40.    A method as in claim 37, wherein mizoribine is released within a time  
2 period of 1 day to 45 days in a vascular environment.

1                   41.    A method as in claim 37, wherein mizoribine is released within a time  
2 period of 7 days to 21 days in a vascular environment.

1                   42.    A method as in claim 37, further comprising releasing at least one  
2 other substance in addition to mizoribine simultaneously with mizoribine release.

1                   43.    A method as in claim 37, further comprising releasing at least one  
2 other substance in addition to mizoribine sequentially with mizoribine release.

1                   44.    A method as in claim 42 or 43, wherein the at least one additional  
2 substance is an immunosuppressive substance selected from the group consisting of  
3 rapamycin, mycophenolic acid, riboflavin, tiazofurin, methylprednisolone, FK 506, zafurin,  
4 and methotrexate.

1                   45.    A method as in claim 37, wherein the releasing comprises delaying  
2 substantial release of mizoribine for at least one hour following implantation of the  
3 prosthesis.

1                   46.    A method as in claim 45, wherein delaying release comprises slowing  
2 release from a reservoir with a material that at least partially degrades in a vascular  
3 environment over said one hour.

1                   47.    A method as in claim 45, wherein delaying release comprises slowing  
2 release with a matrix that at least partially degrades in a vascular environment over said one  
3 hour.

1                   48.    A method as in claim 45, wherein delaying release comprises slowing  
2 release with a nondegradable matrix that allows diffusion of mizoribine through the  
3 nondegradable matrix after said one hour.

1                   49.    A method as in claim 45, wherein delaying release comprises slowing  
2 release with a rate limiting barrier that allows diffusion of mizoribine through the barrier after  
3 said one hour.

1                   50.    A method as in any one of claims 47-49, wherein the prosthesis is  
2   coated with the matrix or barrier by spraying, dipping, deposition, or painting.

1                   51.    A method as in claim 37, wherein the prosthesis incorporates  
2   mizoribine by coating, spraying, dipping, deposition, chemical bonding, or painting  
3   mizoribine on the prosthesis.

1                   52.    A method for inhibiting restenosis in a blood vessel following  
2   recanalization of the blood vessel, said method comprising:

3                   implanting a vascular prosthesis in the blood vessel; and  
4                   releasing mizoribine and at least one other substance in addition to mizoribine  
5   from the prosthesis when implanted in the blood vessel.

1                   53.    A method as in claim 52, wherein the at least one additional substance  
2   is an immunosuppressive substance selected from the group consisting of rapamycin,  
3   mycophenolic acid, riboflavin, tiazofurin, methylprednisolone, FK 506, zafurin, and  
4   methotrexate.

1                   54.    A method as in claim 53, wherein the immunosuppressive substance is  
2   mycophenolic acid.

1                   55.    A method as in claim 53, wherein the immunosuppressive substance is  
2   methylprednisolone.

1                   56.    A method as in claim 55, wherein mizoribine is released within a time  
2   period of 1 day to 45 days and methylprednisolone is released within a time period of 2 days  
3   to 3 months.

1                   57.    A method as in claim 52, wherein the at least one additional substance  
2   comprises at least one agent selected from the group consisting of anti-platelet agent, anti-  
3   thrombotic agent, and IIb/IIIa agent.

1                   58.    A method as in claim 52, wherein mizoribine and the at least one  
2   additional substance are released simultaneously.

1                   59.    A method as in claim 52, wherein mizoribine and the at least one  
2   additional substance are released sequentially.